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News Release

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Data from ARANOTE trial presented as a late-breaking oral presentation at the 2024 ESMO Congress:

Darolutamide plus androgen deprivation therapy significantly reduced the risk of radiological progression or death by 46% compared to placebo plus ADT in patients with metastatic hormone-sensitive prostate cancer

- Results from the pivotal Phase III ARANOTE trial evaluating darolutamide plus androgen deprivation therapy (ADT) showed a statistically significant increase in radiological progression-free survival (rPFS) compared to placebo plus ADT in patients with metastatic hormone-sensitive prostate cancer
- Darolutamide plus ADT now has positive data both with and without docetaxel based on two pivotal Phase III studies in metastatic hormone-sensitive prostate cancer
- Safety analysis reconfirms the established tolerability profile of darolutamide as observed in the ARAMIS and ARASENS trials
- The results have also been simultaneously published in *The Journal of Clinical Oncology*

Abstract: LBA68

Berlin, September 16, 2024 – Results from the Phase III ARANOTE trial have shown that darolutamide plus androgen deprivation therapy (ADT) significantly reduced the risk of radiological progression or death by 46% compared to placebo plus ADT (HR 0.54; 95% CI 0.41–0.71; P<0.0001), in patients with metastatic hormone-sensitive prostate cancer (mHSPC). Consistent benefits in rPFS were observed across pre-specified subgroups, including patients with high- and low-volume mHSPC. Treatment emergent adverse event (TEAEs) were low and similar between treatment groups. The results were presented at the 2024 ESMO Congress and have been simultaneously published in *The Journal of Clinical Oncology*.

“Each diagnosis of metastatic hormone-sensitive prostate cancer is unique, shaped by factors such as age, comorbidities, and patient preferences. Each patient therefore requires a tailored treatment approach that thoughtfully addresses these key considerations”, said Fred Saad, Professor and Chairman of Surgery and Director of Genitourinary Oncology at the University of Montreal, and Principal Investigator of the ARANOTE trial. “With the positive results from ARANOTE, in addition to the ARASENS data, darolutamide has now demonstrated strong efficacy and safety both with and without chemotherapy in mHSPC. If regulatory approval is granted, physicians will have greater flexibility to tailor treatment to individual patient needs.”

“The ARANOTE trial was designed to investigate darolutamide with ADT alone to provide an additional option for patients with mHSPC”, said Christian Rommel, Ph.D., Head of Research and Development at Bayer’s Pharmaceuticals Division. “Supported by our robust clinical development program, darolutamide has the potential to become a foundational therapy in prostate cancer. Our focus is to deliver this potential new treatment option to patients and physicians as quickly as possible.”

Bayer plans to submit the data from the ARANOTE trial to health authorities globally to support the expanded use of darolutamide in patients with mHSPC. Darolutamide is already approved for the treatment of patients with mHSPC under the brand name Nubeqa™ in combination with ADT and docetaxel in more than 80 markets, and for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC), who are at high risk of developing metastatic disease, in over 85 countries around the world. The product is developed jointly by Bayer and Orion Corporation, a globally operating Finnish pharmaceutical company.

Detailed results from ARANOTE

Darolutamide plus ADT significantly reduced the risk of radiological progression or death by 46% (HR 0.54; 95% CI 0.41–0.71; P<0.0001), compared with placebo plus ADT. Consistent benefits in rPFS were observed across patient subgroups, including high- and low-volume mHSPC, with a risk reduction by 40% and 70% (HR 0.60; 95% CI 0.44-0,80 and HR 0.30; 95% CI 0.15-0.50), respectively. An analysis of immature data of overall survival (OS), which measures the time from treatment until death from any cause, was suggestive of a potential benefit with darolutamide plus ADT (HR=0.81, 95% CI 0.59-1.12) vs placebo plus ADT. The ARANOTE data also suggested numerical clinical benefits

across all other secondary endpoints including delaying the time to CRPC (HR 0.40; 95% CI, 0.32–0.51), time to PSA progression (HR 0.31; 95% CI 0.23–0.41), time to pain progression (HR 0.72; 95% CI, 0.54–0.96), and time to initiation of subsequent systemic therapy (HR 0.40; 95% CI, 0.29–0.56), compared to placebo plus ADT.

Incidences of treatment-emergent adverse events (TEAEs) were low (most were grade 1 or 2) and similar between treatment arms, and treatment discontinuations due to TEAEs were lower in patients receiving darolutamide compared to placebo plus ADT (6.1% vs 9.0%). The most frequently reported AEs (incidence of ≥10%) for darolutamide plus ADT vs placebo, were anemia (20.4% and 17.6%, respectively), arthralgia (12.4% and 11.3%, respectively), and urinary tract infections (11.7% and 7.7%, respectively). The incidence of fatigue was lower with darolutamide plus ADT vs placebo (5.6% and 8.1%, respectively). Incidence of TEAEs of interest were minimal between treatment arms, with a difference of ≤2% for coronary artery disorders, cardiac arrhythmias, and vasodilation/flushing.

About the ARANOTE Trial

The ARANOTE trial is a randomized, double-blind, placebo-controlled Phase III study designed to assess the efficacy and safety of darolutamide plus ADT in patients with mHSPC. 669 patients were randomized 2:1 to receive either 600mg of darolutamide twice daily or placebo in addition to ADT.

The primary endpoint of this study is rPFS, measured as time from randomization to date of first documented radiological progressive disease or death due to any cause, whichever occurs first. Secondary endpoints include overall survival (time to death from any cause), time to first castration-resistant event, time to initiation of subsequent anti-cancer therapy, time to prostate-specific antigen (PSA) progression, PSA undetectable rates, time to pain progression, and safety assessments.

About darolutamide (Nubeqa™)

Darolutamide is an oral androgen receptor inhibitor (ARi) with a distinct chemical structure that binds to the androgen receptor with high affinity and exhibits strong antagonistic activity, thereby inhibiting the receptor function and the growth of prostate cancer cells. The low potential for blood-brain barrier penetration for darolutamide is supported by preclinical models and neuroimaging data in healthy humans. This is also supported by the overall low incidence of central nervous system (CNS)-related adverse events (AEs)

compared to placebo as seen in the ARAMIS Phase III trial and the maintained verbal learning and memory observed in the darolutamide arm of the Phase II ODENZA trial.

ARANOTE is part of a robust clinical development program investigating darolutamide across various stages of prostate cancer, which includes the Phase III ARASTEP trial evaluating darolutamide plus ADT compared to ADT alone in hormone-sensitive high-risk biochemical recurrence (BCR) prostate cancer, who have no evidence of metastatic disease by conventional imaging and a positive PSMA PET/CT at baseline. Furthermore, darolutamide is also being investigated in the collaborative Phase III DASL-HiCaP (ANZUP1801) trial led by the Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP). The study evaluates darolutamide as an adjuvant treatment for localized prostate cancer with very high risk of recurrence.

About Metastatic Hormone-Sensitive Prostate Cancer

Prostate cancer is the second most common cancer in men and the fifth most common cause of cancer death in men worldwide.[1] In 2022, an estimated 1.5 million men were diagnosed with prostate cancer, and about 397,000 died from the disease worldwide.[1] Prostate cancer diagnoses are projected to increase from 1.4 million annually in 2020 to 2.9 million by 2040.[2]

At the time of diagnosis, most men have localized prostate cancer, meaning their cancer is confined to the prostate gland and can be treated with curative surgery or radiotherapy. mHSPC is a stage in the disease where the cancer has spread outside of the prostate to other parts of the body. Up to 10% of men will present with mHSPC when first diagnosed.[3,4,5] For patients with mHSPC, ADT is the cornerstone of treatment, often in combination with chemotherapy docetaxel and/or an androgen receptor inhibitor (ARi). Despite treatment, most men with mHSPC will eventually progress to metastatic castration-resistant prostate cancer (mCRPC), a condition with limited survival.

About Prostate Cancer at Bayer

Bayer is committed to delivering science for a better life by advancing a portfolio of innovative treatments. The company has the passion and determination to develop new medicines that help improve and extend the lives of people living with cancer. Prostate cancer is the second most commonly diagnosed cancer in men[2] and a key area of focus for Bayer. The company's franchise includes two products on the market (Nubeqa™ and

Xofigo™) and several compounds in development. Bayer is focused on addressing the unique needs of patients with prostate cancer, providing treatments that extend their lives throughout the different stages of the disease and allowing them to continue with their everyday activities, so that patients can live longer, better lives.

About Bayer

Bayer is a global enterprise with core competencies in the life science fields of health care and nutrition. In line with its mission, “Health for all, Hunger for none,” the company’s products and services are designed to help people and the planet thrive by supporting efforts to master the major challenges presented by a growing and aging global population. Bayer is committed to driving sustainable development and generating a positive impact with its businesses. At the same time, the Group aims to increase its earning power and create value through innovation and growth. The Bayer brand stands for trust, reliability and quality throughout the world. In fiscal 2023, the Group employed around 100,000 people and had sales of 47.6 billion euros. R&D expenses before special items amounted to 5.8 billion euros. For more information, go to www.bayer.com.

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